REMARKS/ARGUMENTS

Claims 1-12 remain in the application. Claims 5-11 were previously not examined.

Objections to Claims

The Examiner has objected to claims 5-11 for improper multiple dependency. Subsequently, the Examiner did not further examine claims 5-11. Claims 5-11 have been amended into proper dependent format for further consideration. The claims 1-4, and 12 are objected to for reasons of claim language, which have also be corrected per the Examiner's suggestions.

Claim Rejections 35 USC § 112

The Examiner rejected claims 1-4 and 12 under 35 USC § 112, second paragraph, due to the claim limitation "approved anti-tumor medicament" being vague and indefinite. The Examiner further stated that the specification does not clearly set forth the definition of this limitation explicitly and with clarity. Claims 1-4 and 12 have been amended to replace the phrase "approved antitumor medicament" to "antitumor substance chosen cis-platinum, carboplatinum, oxaliplatinum, bleomycin, doxorubicin, methotrexate, paclitaxel, docetaxel, vincristine, vinblastine, etoposide, teniposide, ifosfamide, cyclophosphamide, 5-fluorouracil, fludarabin, gemcitabin and cytarabin" as disclosed in the specification. No new matter has been added.

Claim Rejections under 35 USC § 102(b):

The Examiner has given several 35 USC § 102(b) rejections stating that the invention is substantially disclosed in the following references.

First, claims 1-4 and 12 are rejected under 35 USC § 102(b) as being anticipated by Nickel *et al.*, US 6,093,704.

Second, claims 1-4 and 12 are rejected under 35 USC § 102(e) as being anticipated by Nickel *et al.*, US 6,696,428.

And finally, claims 1,3, 4 and 12 are rejected under 35 USC § 102(b) as being anticipated by Nössner *et al.*, US 6,172,050. The Examiner states that specific compounds that fall within the scope of the present claims can be found in Examples 5 and 18-21, as well as claims 5 and 6, of Nössner *et al.*

Under 35 USC §102, a claim can be rejected only if each element of the claim is disclosed in a single prior art reference. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Nickel *et al.*, (US 6,093,704), Nickel *et al.*, (US 6,696,428), and Nössner *et al.*, (US 6,172,050), fail to teach or suggest, either expressly or inherently, each and every element of the claimed invention. The scope of the presently claimed invention is the administration of the expressly claimed alkylphosphocholines in combination with antitumor medicaments, more specifically suitable cytostatics, for treating benign and malignant tumor diseases. See claims 1 through 12 (as amended). The claimed such combination is novel and none of the cited references describe such a combination. We have verified this by careful review of all the references and did not find any teaching or suggestion to combine the alkylphosphocholines of the references with antitumor medicaments.

Applicants are familiar with all of the patents and that they describe the preparation of alkylphosphocholines or the combination of alkylphosphocholines with dopamine receptor antagonists for reducing side effects. However, Applicants are confident that none of the patents disclose the claimed invention.

Accordingly, Applicants respectfully submit that Nossner *et al.* (US 6,172,050) describes in column 19, lines 48-54 the activity of alkylphosphocholines **alone without** a combined composition or administration with other cytostatics.

In contrast, Nickel *et al.*, (US 6,093,704) describes a composition and method of using alkylphosphocholines, such as miltefosine, in conjunction with an appetite-stimulating dopamine receptor antagonist, such as domperidone or pimozide, to treat the side effect of a decrease in body weight caused by administration of alkylphosphocholines in tumor therapy. Nickel *et al.*, (US 6,093,704), fails to teach the use of alkylphosphocholines in combination with antitumor medicaments, more specifically suitable cytostatics, for treating benign and malignant tumor diseases.

Similarly to Nickel *et al.*, (US 6,093,704), Nickel *et al.*, (US 6,696,428) describes a composition and method of using alkylphosphocholines, such as octadecyl (1,1-dimethylpiperidinio-4-yl)phosphate, in conjunction with an appetite-stimulating dopamine receptor antagonist to treat the side effect of a decrease in body weight caused by administration of the alkylphosphocholine in tumor therapy, wherein the amount of appetite-stimulating dopamine receptor antagonist used is not effective for the treatment of said cancer sensitive to the said alkylphosphocholine. Therefore, Nickel *et al.*, (US 6,696,428) does not anticipate the claimed invention.

Thus, Applicants respectfully submit that the rejection of claims 1-4 and 12 under 35 USC § 102(b) is overcome and withdrawal thereof is requested.

Claim Rejections under 35 USC § 103(a):

The Examiner rejected claims 1, 2, and 12 under 35 USC § 103(a) as being unpatentable over Engel *et al.* (US 5,942,639) in view of Nickel et al., (US 6,093,704). According to the Examiner, Engel *et al.* fails to teach the specified use of these compounds in pharmaceutical compositions. However, Engel *et al.* combined with the teachings of Nickel *et al.*, (US 6,093,704) would make it obvious to modify the alkylphosphocholines disclosed in the Engel *et al.* reference into the present claimed invention.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claimed limitations. The teaching or suggestion to make the claimed combination and the reasonably expectation of success must both be found in the prior art, and not based on an applicant's disclosure in the specification. *See In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991).

Claims 1, 2, and 12 of the presently claimed invention are drawn to the method of using the expressly claimed alkylphosphocholines in combination with any one of a selection of given antitumor medicaments for treating benign and malignant tumor diseases. The Examiner acknowledges that Engel *et al.* fails to teach the specified use of these alkylphosphocholines compounds in pharmaceutical compositions. However, Applicants respectfully disagree that the teachings of Nickel *et al.*, (US 6,093,704) would make it obvious to modify the alkylphosphocholines disclosed in the Engel *et al.* reference into the present claimed invention. As discussed above, Nickel *et al.*, (US 6,093,704) describes a composition and method of using alkylphosphocholines in conjunction with an appetite-stimulating dopamine receptor antagonist to treat the side effect of a decrease in body weight caused by administration of alkylphosphocholines in tumor therapy. Nickel *et al.*, US 6,093,704, fails to teach the use of alkylphosphocholines in combination with antitumor medicaments, more specifically suitable cytostatics, for treating benign and malignant tumor diseases. Even if one of ordinary skill in the art were to use an antitumor compound, such as miltefosine or octadecyl (1,1-dimethylpiperidinio-4-yl) phosphate, disclosed by Nickel *et al.*, for the treatment of cancer, all the claimed limitations would still not taught or suggested because there is no suggestion or motivation to use of alkylphosphocholines in combination with an antitumor substance chosen from cis-platinum, carboplatinum, oxaliplatinum, bleomycin, doxorubicin, methotrexate, paclitaxel, docetaxel, vincristine, vinblastine, etoposide, teniposide, ifosfamide, cyclophosphamide, 5-fluorouracil, fludarabin, gemcitabin and cytarabin for treating benign and malignant tumor diseases. Therefore, a *prima facie* case of obviousness has not been established by the Examiner, and thus, claims 1, 2, and 12 are not rendered unpatentable over Engel *et al.* (US 5,942,639) in view of Nickel et al., (US 6,093,704). Accordingly, the rejection of claims 1, 2, and 12 under 35 U.S.C. § 103(a) are overcome and withdrawal thereof is respectfully requested.

Double Patenting:

The Examiner has rejected claims 1, 3, 4, and 12 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of US 6,172,050. The Examiner acknowledges that "although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and US 6,172,050 claim alkylphosphocholine compounds having anti-tumor activity, wherein the compounds claimed are substantially identical to those claimed in the instant application." The Applicants respectfully traverse the Examiner's nonstatutory double patenting rejection. Applicants submit that the cited patent references are assigned to the company ASTA Medica, which was the former, or predecessor, company of Zentaris (the current assignee of the present invention). Furthermore, the inventor Jürgen Engel is a common inventor in the present application and in all of the cited references used in the 35 USC § 102(b) rejections. However, the Applicants find that the Examiner has failed to make a *prima facie* case of obviousness regarding the use of alkylphosphocholines in combination with antitumor medicaments, more specifically suitable cytostatics, for treating benign and malignant tumor diseases and therefore withdrawal of the double patenting rejection is respectfully requested.

Conclusion:

Based on the foregoing amendments and remarks, favorable consideration and allowance of all of the claims now present in the application are respectfully requested.

Should the Examiner require or consider it advisable that the specification, claims and/or drawings be further amended or corrected in formal respects in order to place the case in condition for final allowance, then it is respectfully requested that such amendment or correction be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing this case to allowance, the Examiner is invited to telephone the undersigned.

The Commissioner is authorized to charge any required fees, including any extension and/or excess claim fees, any additional fees, or credit any overpayment, to Goodwin Procter LLP Deposit Account No. 06-0923.

Respectfully submitted for Applicant,

Ann-Marie Koss (Reg. No. 54,237)
GOODWIN PROCTER LLP
599 Lexington Avenue
New York, NY 10022
(212) 459-7434